

Cobalamin-Responsive Psychosis as the Sole Manifestation of Vitamin B12 Deficiency

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We describe two young Bedouin patients who developed acute psychosis accompanied by features suggestive of organic etiology. They were found to have cobalamin deficiency in the absence of typical neurological or hematological abnormalities. Treatment with anti-psychotic drugs had no effect, but treatment

with vitamin B12 led to a complete recovery. These cases suggest that B12 deficiency can present as an isolated acute psychotic episode. We therefore recommend that vitamin B12 levels be determined in patients with mental and psychiatric disturbances in order to prevent severe and irreversible complications.

The association of vitamin B12 deficiency and neuropsychiatric disorders

has been known since the discovery of the vitamin in the 1940s. Among the main neurological symptoms frequently present in chronic B12 deficiency are posterolateral myelopathy, peripheral neuropathy, and optic atrophy. Accompanying mental disturbances such as dementia (especially in elderly subjects), fatigue, mood disorders and even psychoses have been described. In some instances, the psychiatric disturbances

may occur as the main or sole symptom, in the absence of any neurological or hematological abnormalities [1]. Although the presentation of psychosis alone is considered a rare condition, determination of serum vitamin B12 levels is still recommended as an essential test in the workup of mental status changes.

We report two cases of young, non-vegetarian Bedouin women who presented with severe psychotic symptoms associated with vitamin B12 deficiency. Neither patient displayed any of the typical neurological or hematological abnormalities of the vitamin deficiency.

Patient Descriptions

Case 1

An 18 year old Bedouin woman, with low socioeconomic background, presented with progressive behavior changes for over 5 months. These included psychomotor irritability, insomnia, mood changes and visual hallucinations. She frequently felt suffocated and afraid. The psychiatric examination revealed an anxious, depressed and suspicious young woman, complaining of frequent frightening visual hallucinations about a giant black monster with a horrible face trying to strangle her until she runs away from the house crying and screaming. The initial brief psychiatric rating scale total score was 63. Risperidal (1–3 mg/day) was prescribed.

The general physical examination as well as the laboratory tests – complete blood count, electrolytes, liver and kidney functions, thyroid-stimulating hormone and serum folate levels – were normal. Serum vitamin B12 level was 75 pg/ml (normal levels 157–1,059 pg/ml) and serum homocysteine level 28 M (normal 5–15 M). Neurological examination revealed generalized brisk tendon reflexes, with flexor plantar responses and normal vibration and touch sensations. Both the electroencephalogram and brain computerized tomography scan were normal. The mini-mental status examination revealed mild short memory loss and reduced concentration.

Further investigations to determine the etiology of the deficiency – anti-

parietal cell antibodies, gastrin levels, gastroscopy and Schilling test – were all negative. Dietary evaluation disclosed a very low intake of meat and other animal products.

After 2 months with no benefit, treatment with the anti-psychotic drug was stopped and hydroxycobalamin was instituted. This drug, at doses of 1,000 g intramuscularly (three times a week for 6 weeks followed by weekly injections for an additional 6 weeks), resulted in amelioration of psychotic symptoms within 6 weeks. After 3 months of vitamin replacement the BPRS score was 28, and vitamin B12 level was 2,50 pg/ml accompanied by normalization of homocysteine levels. Follow-up for one year revealed a healthy young woman. She is on continuous treatment with oral hydroxycobalamin, 300 g /day, and her B12 level is 1,500 pg/ml.

Case 2

This patient was a 23 year old Bedouin woman, the oldest of eight brothers, poorly educated and unemployed, divorced for two years and childless. Several years earlier she was diagnosed as having hypothyroidism and was appropriately treated. Over a 4 month period she experienced frequent episodes of diurnal and nocturnal visual hallucinations of unidentified terrifying human images trying to assault her. Occasionally she also heard unrecognized threatening voices. She became very irritable and anxious and suffered from sleep disturbances. Her housework performance and her mental condition progressively deteriorated.

General physical examination was within normal limits. Laboratory evaluation revealed normocytic anemia (hemoglobin 10.5 g/dl) with a mean corpuscular volume of 89 fl, and hematocrit 38; white blood cells count, platelets, electrolytes, and hepatic, renal and thyroid function tests were normal.

Psychiatric examination was consistent with an acute psychosis. The BPRS total score was 58. Treatment with

olanzapine was initiated. Further investigation to rule out an organic etiology was recommended. Neurological examination was normal as was the minimal status examination. Brain CT scan with and without contrast and EEG were normal.

Vitamin B12 level was 95 pg/ml, while folate levels were normal (normal 7.2 ng/ml, range 3.5–16.1), and serum homocysteine level was slightly elevated (19 M). Investigations for vitamin B12 malabsorption including anti-parietal cell antibodies, gastrin levels, gastroscopy and Schilling test were all normal.

Treatment with olanzapine 5–15 mg once daily for 6 weeks brought no satisfactory response and it was stopped. Initiation of intramuscular hydroxycobalamin (1,000 g three times a week for 6 weeks followed by once weekly for a further 6 weeks) resulted in complete recovery within 8 weeks. By 8 weeks of treatment the BPRS total score was 22, vitamin B12 level 1,850 pg/ml and homocysteine 12 M. The patient is still taking 300 g/day of hydroxycobalamin orally and has been in good physical and psychiatric condition for more than a year, with vitamin B12 levels ranging from 1,300 to 2,100 pg/ml.

Comment

We describe two young Bedouin women with progressive psychiatric disorders that lasted for several months, with prominent depression, delirium, agitation and frequent frightening visual hallucinations. The psychiatric examination of both patients revealed acute psychoses with no personal or family history of psychiatric illness – all these features suggesting an organic etiology. Diagnostic workup disclosed profound vitamin B12 deficiency associated with elevated serum homocysteine in both patients as well as mild normocytic anemia in one. The patients did not show macrocytic anemia or folate deficiency. The most likely explanation for the absence of macrocytosis lies in the high levels of serum folate, which can

BPRS = Brief Psychiatric Rating Scale

EEG = electroencephalogram

correct the hematological abnormalities but not the neuropsychiatric disturbances. The low iron levels in the second patient could account for her normocytic anemia [2]. In both patients, neurological examination failed to reveal any of the typical symptoms of vitamin B12 deficiency. The response to B12 replacement while anti-psychotic drugs were ineffective further supports B12 deficiency as the cause of these psychotic episodes.

Mental disturbances due to vitamin B12 deficiency have been reported previously as the chief or sole symptom [1], occasionally even preceding the decrease of cobalamin in the serum. Frank psychosis related to vitamin B12 deficiency, however, is considered very rare and has received little attention in the literature. A possible mechanism for psychotic behavior was suggested by Hutto [3], who reported that cobalamin and folate participate in the synthesis of monoamine neurotransmitters in the brain by increasing BH4 (tetrahydrobiopterin) synthesis.

Further tests in our patients failed to disclose evidence for vitamin malabsorption, suggesting that the deficiency was probably dietary. Although these women were not vegetarians, dietary analysis showed that their daily diet was based predominantly on bread, vegetables and canned food, with a minimal intake of

meat or dairy products, which are the sole dietary sources of vitamin B12. These two patients are part of the Bedouin population in southern Israel that was found to harbor extremely high rates of symptomatic dietary vitamin B12 deficiency [4].

Treatment for vitamin B12 deficiency is described as simple, uncomplicated and very helpful, especially when the deficiency is diagnosed early and the appropriate treatment instituted promptly. Our patients were treated with anti-psychotic drugs for 2 months without any benefit and the treatment was stopped. After substitution with intramuscular injections of hydroxycobalamin, the effect was observed within 6–8 weeks after initiation of therapy. Similarly, the two patients described by Evans et al. [5] also showed improvement after several weeks, even though their initial response was more dramatic. Both our patients are currently receiving oral hydroxycobalamin (300 g/day), and after a year of follow-up have maintained their mental health. The therapeutic protocol we used was entirely empirical, as there are no controlled studies or recommendations of optimal therapy for dietary vitamin B12 deficiency. We contend however, that prevention would have been the most effective approach. These two cases further underlie the need to devise effective dietary supple-

mentation of vitamin B12 for low income populations.

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